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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,071	01/08/2001	Karl Tryggvason	TRV 20014 P	6472

20306 7590 08/21/2003

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EXAMINER
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HINES, JANA A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 08/21/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Applicant(s)

09/756,071

Applicant(s)

TRYGGVASON ET AL.

Examiner

Ja-Na Hines

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 12-17 is/are pending in the application.
- 4a) Of the above claim(s) 4-6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 12-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

<b>Notice of References Cited</b>	Application/Control No. 09/756,071	Applicant(s)/Patent Under Reexamination TRYGGVASON ET AL.	
	Examiner Ja-Na A Hines	Art Unit 1645	Page 1 of 1

**U.S. PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

**FOREIGN PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
*	U	Giannelli et al. 1997. Science. vol. 277: 225-228.
	V	
	W	
	X	

\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 29, 2003 has been entered.

### ***Amendment Entry***

2. The amendment filed May 29, 2003 has been entered. Claim 1 has been amended. Claims 12-17 have been newly added. Claims 2-3 and 7-11 have been cancelled. Claims 1 and 12-17 are under consideration in office action.

A complete reply to the rejection must include cancellation of nonelected claims 4-6 or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Information Disclosure Statement***

3. The information disclosure statement filed May 29, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. PTO-Form 1449 has been placed in the application file, but the information referred to therein has not been considered.

***Withdrawal of Rejections***

4. The following rejections have been withdrawn in view of applicants' amendments:

a) The written description rejection of claims 1-3 and 7-11 under 35 U.S.C. 112, first paragraph; and

b) The enablement rejection of claims 1-3 and 7-11 under 35 U.S.C. 112, first paragraph.

***Response to Arguments***

5. Applicant's arguments with respect to claims 1 and 12-17 have been considered but are moot in view of the new ground(s) of rejection.

***New Grounds for Rejection***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method for reducing cell migration, comprising contacting the gamma2 domain III of laminin-5 domain of epithelium derived cells to IgG antibodies against gamma2 domain III of laminin-5 to reduce the ability of

Art Unit: 1645

the cell to migrate, does not reasonably provide enablement for a method for inhibiting cell migration, comprising exposing cells to antibodies against gamma2 domain III of laminin-5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a method for inhibiting cell migration, comprising exposing cells to antibodies against gamma2 domain III of laminin-5. Dependant claims are drawn to cells derived from epithelium, cells comprising tumor cells, the exposure occurs either in vitro or in vivo and that antibodies are either monoclonal or polyclonal. Applicants' point to pages 35-36 as support for the method of inhibiting cell migration using antibodies against the gamma2-domain III chain of lamin-5, yet this fails to adequately support the claims.

The specification at page 35 teaches that the cell migratory role of gamma2 chain of laminin-5 was examined for the KLN-205 cells in vitro. Polyclonal IgG against gamma2 domain III of laminin-5 decreased migration to about 35 to 45% of that observed with the preimmune IgG. See also Figure 7. The in vitro results show cell migration decreased to about 35-45%; furthermore the use of both antibodies inhibited migration to about 50%. The antibodies against gamma2 domain III of laminin-5 will only inhibit the migration of specific cells, such as epithelium derived cells, not any cell type. The art teaches that the migration ability is dose dependant with respect to the amount of antibody used to cause inhibition, yet there is no requirement that a particular amount of antibody be used.

There are no in vivo experiments that teach a method for inhibiting cell migration, comprising exposing cells to antibodies against gamma2 domain III of laminin-5 by exposing an invasive carcinoma to anti-gamma2 chain antibodies against the gamma2-domain III of lamin-5. There is no teaching of complete inhibition and it is noted that inhibiting cell migration is significantly broader than a reduction of cell migration by 35-50%. Thus there are no examples of the claimed method and applicants have not pointed to support in the specification that supports the claimed methods. There are no in vivo examples. There are no working examples of using the method for inhibiting cell migration, solely comprising an exposure step. None of these considerations have been contemplated in the specification, and in absence of these considerations, the rejection is maintained.

In absence of further guidance or support from Applicants, the skilled artisan would have to discover what the appropriate other antibodies, reagents and method steps would be. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use of the claimed method. The claimed method would not predictably result in an enabled method for inhibition. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict a method that would result in the desired method for intervention. Accordingly, one of skill in the art would be required to perform undue experimentation. Therefore, applicants'

Art Unit: 1645

amendments have not overcome the rejection and one skilled in the art could not make and/or use the invention without undue experimentation.

7. Claims 1 and 12-17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: there is no contact step which contacts the antibody to the gamma2-domain III of laminin-5, which allow for some inhibition of cell migration.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1 and 12-14, 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Giannelli et al (1997).

The claims are drawn to a method for inhibiting cell migration, comprising exposing cells to antibodies against gamma2 domain III of laminin-5. Dependant claims are drawn to cells derived from epithelium, cells comprising tumor cells, the exposure occurs either in vitro or in vivo and that antibodies are either monoclonal or polyclonal.

Giannelli et al., teach that laminin-5 is essential for the adhesion of epithelial cells to basement membranes and promotes migration (page 225). A transwell migration



Art Unit: 1645

assay was performed on normal human breast epithelial cells (HUMEC) and nontumorigenic breast cell lines (MCF10) (page 225). Antibodies to a Laminin-5 receptor blocked both HUMEC and MCF10 adhesion to laminin-5 as well as migration on cleaved laminin-5 (page 227). Several monoclonal antibodies, CM6 and MIG1 inhibited migration on laminin-5 in a dose-dependant manner. Thus the authors teach exposing epithelium derived cells, such as HUMEC and MCF10, to antibodies against gamma2 domain III of laminin-5 that inhibit migration. Giannelli et al., noted that gamma2 was not found in either quiescent tissues or tongue and mammary tissues from a sexually immature rat (page 227). The authors' also explored laminin-5 heterodimers containing cleaved gamma2 fragments from cells of mouse skin carcinoma and mammary tissue from a pregnant rat and developed gamma2 specific antibodies (page 227). See also figure 4.

Therefore, Giannelli et al., teach an in vitro method for inhibiting cell migration, comprising exposing epithelium derived cells to monoclonal antibodies against gamma2 domain III of laminin-5.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

Art Unit: 1645

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines 

August 13, 2003

  
LYNETTE R. F. SMITH  
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